

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US98/25422

A. CLASSIFICATION OF SUBJECT MATTER

IPC(6) : A61K 39/395, 39/385

US CL : 424/143.1, 193.1

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

U.S. : 424/143.1, 193.1

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)
APS, DIALOG

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	TERSKIKH, A.V. et al. "Peptabody": A new type of high avidity binding protein. Proc. Natl. Acad. Sci. USA. March 1997, Vol. 94, pages 1663-1668, see entire document.	1-36
Y	EP 0 459 577 A2 (MERCK & CO. INC.) 04 December 1991, see entire document.	1-33
Y	WELPLY, J.K. et al. A Peptide Isolated by Phage Display Binds to ICAM-1 and Inhibits Binding to LFA-1. PROTEINS: Structure, Function, and Genetics. 1996, Vol. 26, pages 262-270, see entire document.	1-12, 19-23, 25-27, 29-31, 33-35

Further documents are listed in the continuation of Box C.

See patent family annex.

* Special categories of cited documents	*T*	later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
A document defining the general state of the art which is not considered to be of particular relevance	*X*	document of particular relevance, the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
B earlier document published on or after the international filing date	*Y*	document of particular relevance, the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art
L document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)		
O document referring to an oral disclosure, use, exhibition or other means	*&*	document member of the same patent family
P document published prior to the international filing date but later than the priority date claimed		

Date of the actual completion of the international search 26 FEBRUARY 1999	Date of mailing of the international search report 15 MAR 1999
---	---

Name and mailing address of the ISA/US Commissioner of Patents and Trademarks Box PCT Washington, D.C. 20231 Facsimile No. (703) 305-3230	Authorized officer DONNA C. WORTMAN, Ph.D. Telephone No. (703) 308-0196
---	---

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US98/25422

C (Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	HOFER, F. et al. Members of the low density lipoprotein receptor family mediate cell entry of a minor-group common cold virus. Proc. Natl. Acad. Sci. USA. March 1994, Vol. 91, pages 1839-1842, see entire document.	1-6, 13-18, 20-22, 24-26, 28-30, 32-34, 36
Y	HODITS, R. A. et al. An Antibody Fragment from a Phage Display Library Competes for Ligand Binding to the Low Density Lipoprotein Receptor Family and Inhibits Khinovirus Infection. The Journal of Biological Chemistry. 13 October 1995, Vol. 270, No. 41, pages 24078-24085, see entire document.	1-6, 13-18, 20-22, 24-26, 28-30, 32-34, 36

ATTENT COOPERATION TRE. NY

PCT

NOTIFICATION OF ELECTION

(PCT Rule 61.2)

From the INTERNATIONAL BUREAU

To:

Assistant Commissioner for Patents
 United States Patent and Trademark
 Office
 Box PCT
 Washington, D.C.20231
 ÉTATS-UNIS D'AMÉRIQUE

in its capacity as elected Office

Date of mailing (day/month/year) 31 August 1999 (31.08.99)	
International application No. PCT/US98/25422	Applicant's or agent's file reference 238/270 PCT
International filing date (day/month/year) 30 November 1998 (30.11.98)	Priority date (day/month/year) 01 December 1997 (01.12.97)
Applicant FANG, Fang	

1. The designated Office is hereby notified of its election made:

in the demand filed with the International Preliminary Examining Authority on:

15 June 1999 (15.06.99)

in a notice effecting later election filed with the International Bureau on:

2. The election was

was not

made before the expiration of 19 months from the priority date or, where Rule 32 applies, within the time limit under Rule 32.2(b).

The International Bureau of WIPO 34, chemin des Colombettes 1211 Geneva 20, Switzerland Facsimile No. (41-22) 740.14.35	Authorized officer Marie-José Devillard Telephone No. (41-22) 338.83.38
--	---

PATENT COOPERATION TREATY

REC'D 05 JUL 2000
WFO

PCT

RECEIVED

09555446

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

SEARCH CENTER 1600/2800

Applicant's or agent's file reference 238/270 PCT	FOR FURTHER ACTION See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)	
International application No. PCT/US98/25422	International filing date (day/month/year) 30 NOVEMBER 1998	Priority date (day/month/year) 01 DECEMBER 1997
International Patent Classification (IPC) or national classification and IPC IPC(7): A61K 39/395, 39/385 and US Cl.: 424/143.1, 193.1		
Applicant CFY BIOMEDICALS, INC.		

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.
2. This REPORT consists of a total of <u>4</u> sheets.
<input type="checkbox"/> This report is also accompanied by ANNEXES, i.e., sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority. (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT). These annexes consist of a total of <u>0</u> sheets
3. This report contains indications relating to the following items:
I <input checked="" type="checkbox"/> Basis of the report
II <input type="checkbox"/> Priority
III <input type="checkbox"/> Non-establishment of report with regard to novelty, inventive step or industrial applicability
IV <input type="checkbox"/> Lack of unity of invention
V <input checked="" type="checkbox"/> Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
VI <input type="checkbox"/> Certain documents cited
VII <input type="checkbox"/> Certain defects in the international application
VIII <input type="checkbox"/> Certain observations on the international application

Date of submission of the demand 15 JUNE 1999	Date of completion of this report 25 MAY 2000
Name and mailing address of the IPEA/US Commissioner of Patents and Trademarks Box PCT Washington, D.C. 20231	Authorized officer DONNA C. WORTMAN, PH.D. 
Facsimile No. (703) 305-3230	Telephone No. (703) 308-0196

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No.

PCT/US98/25422

RECEIVED

I. Basis of the report

1. With regard to the **elements** of the international application:*

the international application as originally filed

PCT CENTER 1600/2900

the description:

pages 1-20

, as originally filed

pages NONE

, filed with the demand

pages NONE

, filed with the letter of _____

the claims:

pages 21-26

, as originally filed

pages NONE

, as amended (together with any statement) under Article 19

pages NONE

, filed with the demand

pages NONE

, filed with the letter of _____

the drawings:

pages NONE

, as originally filed

pages NONE

, filed with the demand

pages NONE

, filed with the letter of _____

the sequence listing part of the description:

pages NONE

, as originally filed

pages NONE

, filed with the demand

pages NONE

, filed with the letter of _____

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.

These elements were available or furnished to this Authority in the following language _____ which is:

the language of a translation furnished for the purposes of international search (under Rule 23.1(b)).

the language of publication of the international application (under Rule 48.3(b)).

the language of the translation furnished for the purposes of international preliminary examination (under Rules 55.2 and/or 55.3).

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing

contained in the international application in printed form

filed together with the international application in computer readable form

furnished subsequently to this Authority in written form

furnished subsequently to this Authority in computer readable form

The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.

The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. The amendments have resulted in the cancellation of:

the description, pages NONE

the claims, Nos. NONE

the drawings, sheets/fig. NONE

5. This report has been drawn as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).**

* Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rules 70.16 and 70.17).

**Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No.

PCT/US98/25422

V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1 statement

Novelty (N)	Claims 1-36	YES
	Claims <u>NONE</u>	NO
Inventive Step (IS)	Claims <u>NONE</u>	YES
	Claims 1-36	NO
Industrial Applicability (IA)	Claims 1-36	YES
	Claims <u>NONE</u>	NO

2 citations and explanations (Rule 70.7)

Claims 1-18 and 34-36 lack an inventive step under PCT Article 33(3) as being obvious over Terskikh et al. in view of Welply et al. and Hodits et al. Terskikh et al. disclose the synthesis and the advantages of high avidity multivalent binding proteins termed "peptabodies" which can also be combined so as to form heteropentamers with bispecific binding properties. Terskikh et al. do not teach "peptabodies" that are specific for ICAM-1 and/or LDL receptors. Welply et al. describe isolation of a peptide from a phage display library that binds to ICAM-1, which is known to function as a receptor for a rhinovirus coat protein. Hodits et al. disclose isolation of an antibody fragment from a phage display library that binds to LDL receptor, also known to function as a rhinovirus receptor. It would have been obvious to one of ordinary skill in the art to construct the "peptobody" of Terskikh et al. that is specific for the ICAM-1 rhinovirus receptor of Welply et al. and/or specific for the LDL receptor rhinovirus receptor of Hodits et al. because Terskikh et al. disclose the "peptobody" construction to be generally applicable for making high avidity binding proteins that are either monospecific or bispecific.

Claims 19-33 lack an inventive step under PCT Article 33(3) as being obvious over Terskikh et al., Welply et al., and Hodits et al., further in view of EP 0 459 577. The teachings of Terskikh et al., Welply et al., and Hodits et al. are set forth above. Hodits et al. additionally teaches that the peptide that specifically binds to LDL receptor inhibits rhinovirus infection. EP 0 459 577 discloses a recombinant binding portion of a monoclonal antibodies that specifically binds to ICAM-1 and blocks rhinovirus attachment to cells. It would have been obvious to one of ordinary skill in the art to use the "peptobody" of Terskikh et al. that is specific for the ICAM-1 rhinovirus receptor of Welply et al. and/or that of EP 0 459 577, that is specific for the LDL receptor rhinovirus receptor of Hodits et al. to prevent rhinovirus infection because Hodits et al. and EP 0 459 577 disclose that peptides that bind to ICAM-1 and/or to LDL receptor prevent rhinovirus attachment and infection.

(Continued on Supplemental Sheet.)

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No.

PCT/US98/25422

Supplemental Box

(To be used when the space in any of the preceding boxes is not sufficient)

Continuation of: Boxes I - VIII

Sheet 10

V. 2. REASONED STATEMENTS - CITATIONS AND EXPLANATIONS (Continued):

Claims 1-36 meet the criteria set out in PCT Article 33(2) because the prior art does not anticipate multivalent recombinant antibodies or peptides that bind to ICAM-1 and/or LDL receptor and prevent rhinovirus infection.

Claims 1-36 meet the criteria for industrial applicability set out in PCT Article 33(4).

----- NEW CITATIONS -----

NONE

*TOWNSEND & TOWNSEND & CREW
RECEIVED PCT
00 JUL 28 AM 10:30
NOTIFICATION OF THE RECORDING
OF A CHANGE*

(PCT Rule 92bis.1 and
Administrative Instructions, Section 422)

Date of mailing (day/month/year)
18 July 2000 (18.07.00)

Applicant's or agent's file reference
19815-1PC

International application No.
PCT/US98/25422

From the INTERNATIONAL BUREAU

To:

WEBER, Kenneth, A.
Townsend and Townsend and Crew LLP
Two Embarcadero Center, 8th floor
San Francisco, CA 94111-3834
ETATS-UNIS D'AMERIQUE

IMPORTANT NOTIFICATION

1. The following indications appeared on record concerning:

the applicant the inventor the agent the common representative

Name and Address
KREUSER, Ed., O.
Lyon & Lyon LLP
Suite 4700
633 West Fifth Street
Los Angeles, CA 90071-2066
United States of America

State of Nationality	State of Residence
Telephone No. (619) 552-8400	
Facsimile No. (213) 955-0440	
Telex/Teletypewriter No.	

2. The International Bureau hereby notifies the applicant that the following change has been recorded concerning:

the person the name the address the nationality the residence

Name and Address
WEBER, Kenneth, A.
Townsend and Townsend and Crew LLP
Two Embarcadero Center, 8th floor
San Francisco, CA 94111-3834
United States of America

State of Nationality	State of Residence
Telephone No. (415) 576-0200	
Facsimile No. (415) 576-0300	
Telex/Teletypewriter No.	

3. Further observations, if necessary:

Please note new reference number.

4. A copy of this notification has been sent to:

<input checked="" type="checkbox"/> the receiving Office	<input type="checkbox"/> the designated Offices concerned
<input type="checkbox"/> the International Searching Authority	<input checked="" type="checkbox"/> the elected Offices concerned
<input checked="" type="checkbox"/> the International Preliminary Examining Authority	<input checked="" type="checkbox"/> other: KREUSER, Ed., O.

The International Bureau of WIPO
34, chemin des Colombettes
1211 Geneva 20, Switzerland

Facsimile No.: (41-22) 740.14.35

Authorized officer

A. Karkachi

Telephone No.: (41-22) 338.83.38

003415413

DMS

PATENT COOPERATION TREATY
 TOWNSEND & TOWNSEND
 & CREW

From the
 INTERNATIONAL PRELIMINARY EXAMINING AUTHORITY

To: KENNETH A. WEBER
 TOWNSEND AND TOWNSEND AND CREW LLP
 TWO EMBARCADERO CENTER, 8TH FLOOR
 SAN FRANCISCO, CALIFORNIA 94111-3834

CO JUL -6 AM 10: 2 PCT

RECEIVED

NOTIFICATION OF TRANSMITTAL OF
 INTERNATIONAL PRELIMINARY
 EXAMINATION REPORT

(PCT Rule 73.1)

Date of Mailing
 (day/month/year)

03 JUL 2000

Applicant's or agent's file reference

~~230/270 PCT~~ 019815 - 1 PC

IMPORTANT NOTIFICATION

International application No.

PCT/US98/25422 ✓

International filing date (day/month/year)

30 NOVEMBER 1998 ✓

Priority Date (day/month/year)

01 DECEMBER 1997 ✓

Applicant

CFY BIOMEDICALS, INC.

1. The applicant is hereby notified that this International Preliminary Examining Authority transmits herewith the international preliminary examination report and its annexes, if any, established on the international application.
2. A copy of the report and its annexes, if any, is being transmitted to the International Bureau for communication to all the elected Offices.
3. Where required by any of the elected Offices, the International Bureau will prepare an English translation of the report (but not of any annexes) and will transmit such translation to those Offices.

4. REMINDER

6-1-00 (undated)

The applicant must enter the national phase before each elected Office by performing certain acts (filing translations and paying national fees) within 30 months from the priority date (or later in some Offices)(Article 39(1))(see also the reminder sent by the International Bureau with Form PCT/IB/301).

Where a translation of the international application must be furnished to an elected Office, that translation must contain a translation of any annexes to the international preliminary examination report. It is the applicant's responsibility to prepare and furnish such translation directly to each elected Office concerned.

For further details on the applicable time limits and requirements of the elected Offices, see Volume II of the PCT Applicant's Guide.

Name and mailing address of the IPEA/US
 Commissioner of Patents and Trademarks
 Box PCT
 Washington, D.C. 20231
 Facsimile No. (703) 305-3230

Authorized officer
 DONNA C. WORTMAN, PH.D.
 Telephone No. (703) 308-0196

[Signature]



INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(51) International Patent Classification ⁶ : A61K 39/395, 39/385		A1	(11) International Publication Number: WO 99/27964									
			(43) International Publication Date: 10 June 1999 (10.06.99)									
<p>(21) International Application Number: PCT/US98/25422</p> <p>(22) International Filing Date: 30 November 1998 (30.11.98)</p> <p>(30) Priority Data:</p> <table> <tr> <td>60/067,119</td> <td>1 December 1997 (01.12.97)</td> <td>US</td> </tr> <tr> <td>60/083,046</td> <td>24 April 1998 (24.04.98)</td> <td>US</td> </tr> <tr> <td>60/090,632</td> <td>25 June 1998 (25.06.98)</td> <td>US</td> </tr> </table> <p>(71) Applicant (<i>for all designated States except US</i>): CFY BIOMEDICALS, INC. [US/US]; 7155-B Calabria Court, San Diego, CA 92122 (US).</p> <p>(72) Inventor; and</p> <p>(75) Inventor/Applicant (<i>for US only</i>): FANG, Fang [CN/US]; 7155-B Calabria Court, San Diego, CA 92122 (US).</p> <p>(74) Agents: CHEN, Anthony, C. et al.; Lyon & Lyon LLP, Suite 4700, 633 West Fifth Street, Los Angeles, CA 90071-2066 (US).</p> <p>(81) Designated States: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, ARIPO patent (GH, GM, KE, LS, MW, SD, SZ, UG, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG).</p>				60/067,119	1 December 1997 (01.12.97)	US	60/083,046	24 April 1998 (24.04.98)	US	60/090,632	25 June 1998 (25.06.98)	US
60/067,119	1 December 1997 (01.12.97)	US										
60/083,046	24 April 1998 (24.04.98)	US										
60/090,632	25 June 1998 (25.06.98)	US										
<p>Published <i>With international search report.</i></p>												

(54) Title: MULTIVALENT RECOMBINANT ANTIBODIES FOR TREATING HRV INFECTIONS

(57) Abstract

The present invention relates to high affinity multivalent recombinant antibodies and multivalent peptides against ICAM-1 and/or LDL receptor and pharmaceutical compositions containing such multivalent antibodies or multivalent peptides. The present invention also relates to methods of using such multivalent antibodies or multivalent peptides to prevent and treat human rhinovirus infection and diseases and pathological conditions associated therewith.

FOR THE PURPOSES OF INFORMATION ONLY

Codes used to identify States party to the PCT on the front pages of pamphlets publishing international applications under the PCT.

AL	Albania	ES	Spain	LS	Lesotho	SI	Slovenia
AM	Armenia	FI	Finland	LT	Lithuania	SK	Slovakia
AT	Austria	FR	France	LU	Luxembourg	SN	Senegal
AU	Australia	GA	Gabon	LV	Latvia	SZ	Swaziland
AZ	Azerbaijan	GB	United Kingdom	MC	Monaco	TD	Chad
BA	Bosnia and Herzegovina	GE	Georgia	MD	Republic of Moldova	TG	Togo
BB	Barbados	GH	Ghana	MG	Madagascar	TJ	Tajikistan
BE	Belgium	GN	Guinea	MK	The former Yugoslav Republic of Macedonia	TM	Turkmenistan
BF	Burkina Faso	GR	Greece	ML	Mali	TR	Turkey
BG	Bulgaria	HU	Hungary	MN	Mongolia	TT	Trinidad and Tobago
BJ	Benin	IE	Ireland	MR	Mauritania	UA	Ukraine
BR	Brazil	IL	Israel	MW	Malawi	UG	Uganda
BY	Belarus	IS	Iceland	MX	Mexico	US	United States of America
CA	Canada	IT	Italy	NE	Niger	UZ	Uzbekistan
CF	Central African Republic	JP	Japan	NL	Netherlands	VN	Viet Nam
CG	Congo	KE	Kenya	NO	Norway	YU	Yugoslavia
CH	Switzerland	KG	Kyrgyzstan	NZ	New Zealand	ZW	Zimbabwe
CI	Côte d'Ivoire	KP	Democratic People's Republic of Korea	PL	Poland		
CM	Cameroon	KR	Republic of Korea	PT	Portugal		
CN	China	KZ	Kazakhstan	RO	Romania		
CU	Cuba	LC	Saint Lucia	RU	Russian Federation		
CZ	Czech Republic	LI	Liechtenstein	SD	Sudan		
DE	Germany	LK	Sri Lanka	SE	Sweden		
DK	Denmark	LR	Liberia	SG	Singapore		